

Determinants of colorectal cancer diagnosis delay in Morocco

Colorectal cancer diagnosis delay

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Abstract

Aim: In Morocco, over the last 10 years, the colon and rectum have remained the third most common localizations of cancer in both sexes. An advanced diagnosis is often correlated with a poorer prognosis and lower survival rates. Additionally, the time to diagnosis is defined as a predictor of stage and survival. Our study aimed to explore the diagnostic delay of colorectal cancer (CRC) and its determinants.

Material and Methods: A retrospective and cross-sectional analytical study was conducted, including all CRC cases admitted to the National Institute of Oncology in Morocco between 2015 and 2016. Sociodemographic, clinical data, as well as data on the care pathway of patients admitted during the 2015–2016 period, were collected. Diagnostic delay was defined as the time interval between the onset of the first symptoms and the date of diagnosis. A quantile regression analysis was applied to determine the factors associated with this delay.

Results: A total of 321 cases of CRC were included. The median diagnostic delay was three months. This delay was longer for rectal cancer than for colon cancer. The median diagnosis delay of CRC was extended by two months in the presence of rectal bleeding (p-value < 0.01).

Discussion: Diagnostic delay was significantly associated with rectal bleeding, despite it being an alarming symptom. This association has been reported in several previous studies.

Keywords

Colorectal Cancer, Delay, Diagnosis, Factors, Morocco

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Introduction

Colorectal cancer (CRC) is a major cause of mortality and morbidity globally [1]. It ranks as the third most common cancer and the fourth leading cause of cancer-related deaths worldwide, with 1.4 million new cases and around 700,000 deaths annually [2]. In recent decades, the incidence of CRC has increased significantly. The number of newly diagnosed CRC cases rose from 783,000 in 1990 to 1,361,000 in 2012 [3]. In terms of geographical distribution, the incidence of this cancer has increased in industrialized countries with a medium or high Human Development Index [2].

Mortality is estimated at 694,000 deaths in both sexes, accounting for 8.5% of the total, with more deaths (52%) occurring in the less developed regions of the world, reflecting a poorer prognosis in these regions [3].

In Morocco, according to data from the cancer registry of the Greater Casablanca region (2013–2017) (Available at: https://www.irc.ma/images/Registre_des_Cancers_de_la_Region_du_Grand_Casablanca_2013-2017.pdf), CRC is the third most common cancer in both sexes, representing 7.7% of cases. Its incidence increases with age, with the 65 to 74 age group being the most affected.

Mortality attributable to CRC was estimated at 2,892 deaths (7.8%) in 2022, according to Globocan estimates (Available at: <https://gco.iarc.fr/today/fact-sheets-populations>).

The Ministry of Health and Social Protection, in collaboration with the Lalla Salma Foundation (FLS), developed a National Cancer Prevention and Control Plan for 2010–2019 (Available at: https://www.contrelecancer.ma/site_media/uploaded_files/PNPCC_-_Axes_strategiques_et_mesures_2010-2019.pdf). The goal of this plan is to reduce cancer-related morbidity and mortality and improve the quality of life for patients and their families.

Diagnosis and treatment are key components of this plan. Research in these areas is crucial for improving quality of care, especially by reducing the time required to access cancer diagnosis and treatment. This delay serves as a critical indicator of care quality and highlights disparities in access. While several studies have investigated delays in managing breast and cervical cancers [4, 5], no research has specifically focused on CRC.

Studies have shown that delays in diagnosis, attributable to both patients and practitioners, are associated with the stage of CRC at the time of diagnosis [6]. Furthermore, survival rates are closely linked to the stage at diagnosis: the five-year survival rate is over 90% for stage I patients but only 10% for those with stage IV CRC [7]. Therefore, reducing diagnostic delays is crucial for improving patient outcomes [8, 9].

In Morocco, where CRC is the third most common cancer in both sexes, there is currently no specific national program, unlike breast and cervical cancers.

This study aimed to describe the delay in the diagnosis of CRC and identify its determinants in patients treated at the National Institute of Oncology Sidi Abdellah (NIO) in Rabat during the 2015–2016 period.

Material and Methods

Design and population of the study

A retrospective, cross-sectional analytical study was conducted

at the NIO, the first hospital specializing in cancer care in Morocco, inaugurated in 1983. The NIO receives approximately 6,000 new patients annually from across the Kingdom, making it an ideal location for this study.

The study population comprised all patients admitted to the NIO between January 2015 and December 2016, regardless of their age, residence or stage of CRC.

Study eligibility criteria

Inclusion criteria:

The subjects included in this study were Moroccan nationals, patients admitted for the management of primary CRC and patients with a diagnosis confirmed by pathological examination.

Exclusion criteria:

Subjects were excluded from this study if they had a personal history of other cancers or if their medical record lacked essential data for this study.

Sampling

Kish's formula was used to calculate the minimum sample size, assuming that 50% of the delays were greater than the median. With an accuracy of 0.05, the minimum required sample size was 246. To account for the high variability in delays and the potential for missing data, the sample size was increased to 365.

Tool and data collection

Information was collected using a data collection sheet, which allowed for the extraction of all relevant medical records for patients who met the inclusion criteria.

Definition of study variables

The collected information included sociodemographic data, clinical data and information on the care pathway.

Diagnostic delay was defined as the time interval between the onset of symptoms and the confirmation of diagnosis through anatomopathological examination.

Management and statistical analysis

The collected data were coded and entered into a pre-established questionnaire developed using Epi Info version 7 software, with input control. Paper-based records were archived with the study documents.

All variables were analyzed after cleaning the database and missing data were reported.

Bivariate analyses were conducted using the Mann-Whitney and Kruskal-Wallis tests. Quantile regression was then performed to identify factors influencing the diagnostic delay.

Data analysis was carried out using Epi Info version 7 and Stata 10 software.

Ethical Approval

This study was approved by the Ethics Committee of Biomedical Research at the Faculty of Medicine and Pharmacy of Rabat (Date: 2018-02-28, No: 36/18).

Results

A total of 321 cases of CRC were included. The median diagnostic delay for CRC was three months (interquartile range: 1.0 – 7.0). When stratified by cancer location, the median delay was two months (interquartile range: 0 to 5 months) for colon cancer and four months (interquartile range: 2 to 10 months) for rectal cancer.

Due to significant variability in the distribution of diagnostic

delays (with extreme values), the delays exhibited an asymmetrical distribution in our study population. Consequently, the analysis of diagnostic delay based on sociodemographic, clinical and organisational factors was conducted by comparing medians, with p-values derived from exact tests, such as the Mann-Whitney and Kruskal-Wallis tests.

The analysis revealed a statistically significant difference (p-value < 0.01) in diagnostic delay between patients with colon cancer and those with rectal cancer. Therefore, we conducted further analyses on all data and by cancer location.

The analysis of CRC diagnostic delay according to sociodemographic characteristics revealed a statistically significant association with sex (p = 0.04). The median diagnostic delay was three months for women and four months for men. In addition, there was a statistically significant difference (p = 0.01) in diagnostic delays between patients from rural and urban areas, with median delays of four months and three months, respectively. Smoking and alcoholism were also statistically associated with diagnostic delay (see Table 4). For other sociodemographic characteristics, no significant dependence on diagnostic time was found, applicable to all

cancer locations.

However, among patients with colon cancer, having a family history of cancer was associated with a longer diagnostic delay (p = 0.01) (see Table 1).

Clinical features such as transit disorders, weight loss, general impairment, tenesmus and the number of clinical signs were associated with CRC diagnostic delay regardless of cancer location. The median diagnostic delay was five months for patients with rectorrhagia and two months for those without (see Table 2).

Analysis by location revealed a significant association between diagnostic delay and signs such as rectorrhagia, abdominal pain, transit disorders, weight loss and general deterioration in cases of colon cancer. In contrast, only rectorrhagia was significantly associated with diagnostic delay in rectal cancer cases (see Table 2).

Regarding CRC stage and diagnostic delay, there was a statistically significant difference between median delays for early-stage (I and II) and late-stage (III and IV) diagnoses: two months for stages I/II and four months for stages III/IV (p = 0.04) (see Table 2).

Table 1. Distribution of diagnosis delay (in months) by sociodemographic factors for patients with CRC admitted to NIO, Morocco, 2015–2016

Variables	N	Colorectal N= 303 Median (25%-75%)	P	N	Colon N= 140 Median (25%-75%)	P	N	Rectum N= 150 Median (25%-75%)	P
Age (Years)									
< 50 years	81	4 (1 - 8)	0,67	37	3 (1 - 6)	0,52	38	5 (2 - 8)	0,7
50 to 74 years	173	4 (1 - 7)		81	2 (1 - 5)		87	5 (2 - 10)	
≥ 75	48	3 (1 - 7)		21	1 (0 - 4)		25	3 (2 - 6)	
Sexe									
Female	157	3 (1 - 6)	0,05	76	2 (0 - 5)	0,37	76	4 (2 - 8)	0,1
Male	146	4 (2 - 8)		64	3 (1 - 5)		74	5 (3 - 11)	
Marital status									
Single	31	4 (2 - 8)	0,3	9	3 (0 - 4)	0,35	17	5 (2 - 10)	0,73
Married	214	3 (1 - 7)		106	2 (1 - 5)		101	5 (3 - 10)	
Divorced	10	2 (1 - 3)		4	1 (0 - 2)		6	3 (1 - 6)	
Widow (er)	36	3 (0 - 8)		18	2 (0 - 4)		17	6 (2 - 10)	
Residence place									
Urbain	201	3 (1 - 6)	0,01	91	2 (0 - 5)	0,14	100	4 (2 - 8)	0,03
Rural	102	4 (2 - 11)		49	3 (1 - 10)		50	5 (3 - 11)	
Health coverage type									
CHI1/Private insurance	57	3 (1 - 6)	0,18	28	2 (0 - 4)	0,17	28	5 (2 - 10)	0,71
MASED2	221	4 (2 - 7)		100	3 (1 - 5)		109	5 (3 - 10)	
Comorbidity									
Yes	93	4 (1 - 10)	0,15	46	3 (1 - 6)	0,29	44	5 (3 - 11)	0,26
No	210	3 (1 - 7)		94	2 (0 - 4)		106	4 (2 - 8)	
Tobacco use									
Yes	43	5 (3 - 10)	0,05	18	4 (2 - 5)	0,11	22	7 (3 - 11)	0,01
No	144	3 (1 - 8)		66	2 (0 - 5)		75	4 (2 - 10)	
Alcoholism									
Yes	6	4 (3 - 5)	0,86	4	4 (2 - 5)	0,79	1	4	0,83
No	176	4 (1 - 8)		77	2 (1 - 5)		94	5 (3 - 11)	
Family history of cancer									
Yes	23	4 (2 - 11)	0,26	7	5 (3 - 18)	0,02	15	3 (1 - 10)	0,46
No	151	3 (1 - 8)		76	2 (0 - 4)		72	5 (3 - 11)	

¹ Compulsory Health Insurance 2 Medical Assistance Scheme for the Economically Disadvantaged

Considering the patient management pathway, the mode of tumor discovery was statistically associated with diagnostic delay. The median diagnostic delay for CRC was four months, excluding patients diagnosed urgently due to complications (see Table 2).

The analysis of factors associated with diagnostic delay, adjusted for significant characteristics identified in the bivariate analysis using quantile regression, revealed a significant association between CRC diagnosis time and factors such as rectorrhagia, transit disorders, weight loss, number of clinical signs and place of endoscopy. Specifically, the median diagnostic delay was statistically longer by two months for patients with rectorrhagia compared to those without (p-value < 0.01), after adjusting for other sociodemographic, clinical and organizational factors (see Table 7). The delay was also extended by about one month in patients who experienced transit problems or weight loss compared to those who did not (p-value < 0.01). Additionally, when patients presented with more than three clinical signs, the median diagnostic delay was

reduced by just over one month compared to those with three or fewer signs (p-value < 0.01) (see Table 3).

After stratifying the diagnosis delay by location, rectorrhagia was found to significantly delay the diagnosis of both colon and rectal cancers by approximately three months, after adjusting for other clinical signs. In cases of colon cancer, the diagnosis was faster if complications required emergency intervention. Conversely, the diagnosis of CRC was delayed by two months when patients presented with non-specific signs of colon cancer (see Table 3).

For rectal cancer, tenesmus was significantly associated with a delay in diagnosis, with a median delay of two months in patients presenting this sign (p-value < 0.01) (see Table 3).

Discussion

Diagnosis delay

In this study, diagnostic delay is defined as the time interval between the onset of the first clinical signs and the diagnosis of CRC. The median delay was three months with considerable

Table 2. Distribution of diagnosis delay (in months) by clinical and organizational factors for CRC patients admitted to NIO, Morocco, 2015–2016

Variables	N	Colorectal N=303 Median (25%-75%)	P	N	Colon N=140 Median (25%-75%)	P	N	Rectum N=150 Median (25%-75%)	P
Stage (TNM1)									
I/II	67	2 (1–6)	0,04	34	2 (1–4)	0,33	30	3 (1–10)	0,18
III/IV	214	4 (2–8)		95	3 (0–5)		110	5 (3–10)	
Rectorrhagia									
Yes	156	5 (3–11)	<0.01	31	5 (2–11)	<0.01	115	5 (3–10)	<0.01
No	147	2 (0–4)		109	2 (0–4)		35	3 (0–5)	
Abdominal pain									
Yes	135	3 (2–8)	0,39	83	3 (1–6)	<0.01	47	5 (3–10)	0,52
No	168	3 (1–7)		57	1 (0–4)		103	4 (2–10)	
Transit disorders									
Yes	118	4 (2–8)	<0.01	55	3 (2–5)	<0.01	58	5 (3–11)	0,09
No	185	3 (0–7)		85	1 (0–4)		92	4 (2–9)	
Weight loss									
Yes	95	5 (3–10)	<0.01	34	5 (2–11)	<0.01	54	5 (3–10)	0,2
No	208	3 (1–6)		106	2 (0–4)		96	4 (2–8)	
Alteration of general condition									
Yes	65	5 (3–8)	0,02	33	4 (2–6)	<0.01	30	6 (3–8)	0,28
No	238	3 (1–7)		107	2 (0–4)		120	4 (2–10)	
Tenesmus									
Yes	57	4 (3–10)	<0.01	2	3 (2–3)	0,88	53	5 (3–10)	0,31
No	246	3 (1–6)		138	2 (0–5)		97	4 (2–9)	
Number of clinical signs									
No signs	10	0 (0–0)	<0.01	9	0 (0–0)	<0.01	1	1	0,24
1 to 3 signs	228	3 (1–7)		106	2 (0–5)		112	4 (2–9)	
Four signs and more	65	4 (3–10)		25	4 (2–8)		37	5 (3–12)	
Discovery mode									
Emergency intervention (occlusion)	69	0 (0–2)	<0,01	56	0 (0–1)	<0,01	13	1 (0–6)	0,02
Presence of warning signs	232	4 (2–7)		84	4 (2–6)		135	5 (3–10)	
Endoscopy location									
NIO2	13	2 (0–5)	0,08	8	2 (0–4)	0,13	4	3 (1–14)	0,31
Public	55	4 (2–8)		16	3 (2–8)		37	4 (2–8)	
Private	151	5 (3–10)		48	4 (2–8)		95	5 (3–10)	

1 T = tumour, N = nodes, M = metastasis 2 National Institute of Oncology

Table 3. Multivariate analysis by quantile regression of time to diagnosis (in months) by sociodemographic, clinical and care pathway factors for CRC patients admitted to NIO, Morocco, 2015–2016

Factors	Colorectal N=204			p	Colon N=83			p	Rectum N=148			p
	Coef	95% CI			Coef	95% CI			Coef	95% CI		
Sex												
Female	Ref								Ref			
Male	0,34	-0,29; 0,96	0,29	-	-	-	-	1	-0,38; 2,38	0,15		
Place of residence												
Urban	Ref								Ref			
Rural	1,57E-08	-0,67; 0,67	1	-	-	-	-	-6,26 e-16	-1,48; 1,48	1		
Health coverage type												
CHI1/Private insurance	Ref											
MASED2	-8,57E-09	-0,77; 0,77	1	-	-	-	-	-	-	-		
Comorbidity												
No	Ref											
Yes	1,03 e-8	-0,68; 0,68	1	-	-	-	-	-	-	-		
Family history of cancer												
No					Ref							
Yes	-	-	-	3	1,87; 4,13	<0,01	-	-	-	-		
Rectorrhagia												
No	Ref				Ref				Ref			
Yes	2	1,29; 2,71	<0,01	2,67	1,83; 3,51	<0,01	3	1,34; 4,65	<0,01			
Abdominal pain												
No												
Yes	-	-	-	-2,73 e-8	-0,63; 0,63	1	-	-	-	-		
Transit disorder												
No	Ref				Ref				Ref			
Yes	1	0,29; 1,71	<0,01	0,67	-0,07; 1,41	0,08	1	-0,43; 2,43	0,17			
Weight loss												
No	Ref				Ref				Ref			
Yes	1,34	0,63; 2,03	<0,01	1,33	0,54; 2,12	<0,01	1	-0,50; 2,50	0,19			
Deterioration of GC4												
No	Ref				Ref							
Yes	0,67	-0,18; 1,51	0,12	0,33	-0,46; 1,13	0,41	-	-	-	-		
Tenesmus												
No	Ref								Ref			
Yes	0,34	-0,41; 1,07	0,38	-	-	-	2	0,55; 3,45	<0,01			
Number of clinical signs												
≤ 3	Ref				Ref							
> 3	-1,34	-2,29; -0,38	<0,01	0,33	-0,66; 1,32	0,5	-	-	-	-		
Mode of discovery												
Emergency intervention	Ref				Ref				Ref			
Presence of warning signs	-8,57 e-9	-0,77; 0,77	1	2	1,28; 2,72	<0,01	1	-1,63; 3,63	0,45			
Endoscopy location												
Public	Ref											
NIO3	-0,67	-2,28; -0,38	0,35	-	-	-	-	-	-	-		
Private	1	0,28; 1,72	<0,01	-	-	-	-	-	-	-		

¹ Compulsory Health Insurance ² Medical Assistance Scheme for the Economically Disadvantaged ³ National Institute of Oncology ⁴ General condition

variability (±7.8 months). This is longer compared to a multicenter study conducted in Spain, which reported a median delay of 36.5 days (interquartile range: 73) [10], and another study in Jordan with an average delay of 5.6 months from symptom onset to the first consultation [11]. In our study, CRC was diagnosed within three months of symptom onset in 50% of cases. The median delay was four months in a study conducted in Spain [12] and 136 days in a cohort from the United Kingdom [13]. It is important to note that a very short diagnostic delay

is not necessarily associated with a better prognosis. Topping et al. (2011) demonstrated in a seven-cohort study comprising 11,720 patients that both primary care delay and secondary care are associated with advanced CRC [14]. Paradoxically, in our population, the diagnostic delay was significantly longer for rectal cancer (median time = four months) compared to colon cancer (median time = two months), despite rectal cancer often presenting with more recognizable symptoms. This observation aligns with previous studies [10,

12, 15, 16]. For instance, in Norway, the diagnosis of rectal cancer was delayed by a month compared to colon cancer [17]. This discrepancy might be attributed to patients' perceptions of proctological examinations. Indeed, a study conducted at Hassan II University Hospital in Fez found that 84% of patients expressed fear or shame regarding this examination [18].

In our study, diagnostic delay was significantly associated with rectal bleeding, despite it being an alarming symptom. This association has been reported in several studies [12, 13, 19]. Previous research suggests that hemorrhoids, which affect 4% to 5% of the adult population [11], cause prolonged diagnostic delays may result from the assumption by patients and/or doctors that rectal bleeding. A longer delay may occur if the patient has both cancer and hemorrhoids. For example, a Danish study found that 63% of CRC patients with rectal bleeding also had hemorrhoids [11]. This may be related to the low positive predictive value of rectal bleeding as a symptom of CRC, ranging from 2.2% to 16%, as reported in a meta-analysis [7]. However, some studies have reported the opposite, noting a shorter diagnostic delay in CRC patients with rectal bleeding [13].

Other clinical signs, such as transit disorders and weight loss for CRC and tenesmus specifically for rectal cancer, were also significantly associated with longer diagnostic times. This, similar to rectal bleeding, could be attributed to the lack of specificity of these symptoms, as several digestive pathologies present with these signs. Some studies report similar findings, while others have not found a significant association [16]. In the absence of a pathognomonic sign for CRC, the risk of late diagnosis remains high, which helps explain the large proportion of late-stage cases observed in our study and in general. Conversely, our results indicated that the presence of multiple signs (more than three) was associated with a faster diagnosis. A previous study has confirmed this association when another one has not found a significant association between the number of clinical signs and diagnosis delay for CRC [12, 13].

The observed effect of clinical signs on the diagnostic delay of CRC partly explains why patients diagnosed through symptom onset and standard diagnostic methods (such as colonoscopy) experienced longer delays compared to those diagnosed during emergency interventions due to obstruction. This relationship between the mode of discovery and diagnostic delay is supported by other studies [12, 20]. Some researchers differentiate their populations based on the mode of tumor discovery [20].

A family history of cancer was found to significantly prolong the median diagnostic delay for colon cancer. This may be attributed to the negative perception of the disease and the fear of being a carrier, influenced by personal experience with a loved one. Although this factor is less studied, some research associates it with the time to treatment, while other studies have not linked it to diagnostic delay [12].

Strengths and limitations of the study

Quantile regression provides a more comprehensive view of variations in diagnostic delays compared to other analytical techniques. Nonetheless, our study has certain limitations. Being retrospective, it is subject to challenges regarding data reliability. Additionally, the lack of information on the timing of the first medical consultation after symptom onset

necessitated treating the entire diagnostic period as a whole, without distinguishing delays caused by patients from those attributable to the healthcare system.

Conclusion

In conclusion, the presence of alarming signs often delays the early diagnosis of CRC rather than facilitating it. Therefore, it is recommended to launch extensive awareness campaigns about presumptive signs for both the general population and healthcare professionals. Additionally, enhancing management capabilities and ensuring the availability of diagnostic tools, such as endoscopy and medical imaging, are crucial. Efforts should also focus on implementing an effective screening program targeting individuals at medium risk.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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